REMARKS

Introduction

Receipt of a non-final Office Action dated June 19, 2007 is acknowledged. In the action, claims 1-3 and 12-14 are rejected as allegedly not enabled and obvious over Treon *et al.*, *Semin. Oncol.*, 27:598-613 (2000), in view of Ohtomo *et al.*, *Biochem. Biophys. Res. Comm.*, 258:583-591 (1999) and Porgador *et al.*, *J. Exp. Med.*, 182:255-260 (1995). The claims are also objected to for informality reasons.

Status of the Claims

In this response, applicants cancelled claims 2, 4-11, 13, and 15-22, amended claims 1, 12 and 14, and added new claim 23. Support for the amended claims can be found throughout the specification, and on page 1, line 30 of the originally filed application. Upon entry of this amendment, claims 1-3, 12, 14 and 23 will be under examination.

Claim Objections

Claims 1 and 12-14 are objected to for being drawn to a non-elected invention. In view of the foregoing claim amendments, applicants believe this rejection is moot.

Rejection of the Claims Under 35 U.S.C. § 112, 1st Paragraph

Claims 1-3 and 12-14 are rejected under 35 U.S.C. § 112, 1st paragraph, because the specification "does not reasonably provide enablement for a cancer vaccine containing as an active ingredient an antigen-specific dendritic cell pulsed by an HM1.24 protein or an HM1.24 peptide." Office action at 3. Applicants respectfully disagree.

The present invention is directed to a cancer vaccine, and not a vaccine in the sense of a preventative measure. In fact, a cancer vaccine is usually used for the treatment of cancer; this description is clear from Evance *et al.*, *Q. J. Med.*, 92:299 (1999), which states that "[u]nlike most vaccines for infectious agents, the goal of [a] cancer vaccine is therapeutic and this can be achieved by activating immune responses against [a] tumor antigen."

Accordingly, an effective cancer vaccine is one in which an immune response is mounted against a tumor antigen, such as the composition of the present invention.

In fact, the working examples demonstrate dendritic cells pulsed with HM1.24 stimulate T cells, and further states that in an ELISpot assay with 5 multiple myeloma patients, T cells had a greater response to HM1.24 loaded PBMCs and autologous plasma cells, than control PBMCs and allogenic tumor cells. See Example 1 of the present application. The other working examples in the application further support the value of HM1.24 loaded dendritic cells as a cancer vaccine.

In view of the teachings in the application, applicants respectfully assert that the specification describes how to make and use a cancer vaccine containing as an active ingredient an antigen-specific dendritic cell pulsed by an HM1.24 protein or peptide.

Rejection of the Claims Under 35 U.S.C. § 103

Claims 1-3 and 12-14 are rejected under 35 U.S.C. § 103 as allegedly obvious over Treon, in view of Ohtomo and Progador. In particular, the claims are rejected because "[i]t would have been *prima facie* obvious . . . to make dendritic cells pulsed with HM1.24 protein or HM1.24 soluble peptide for treating multiple myeloma in view of the teachings of Treno, Ohtomo and Porgador et al." Office action at 9. Applicants respectfully traverse this ground of rejection.

The Supreme Court recently addressed the appropriate standard for obviousness in *KSR International Co. v. Teleflex Inc.*, No. 04-1350 (U.S., April 30, 2007). The Court explained that the proper question for evaluating obviousness is "whether there was an apparent reason to combine the known elements in the fashion claimed." *KSR*, slip op. at 14. Here, the record evidences no such reason.

Treon describes a therapeutic method for plasma cell tumors such as myeloma using dendritic cells pulsed with cancer antigen of myeloma-related peptide. However, as the Examiner recognizes, "Treon et al. do not specifically describe dendritic cells pulsed with HM1.24 protein of HM1.24 soluble peptide."

Ohtomo et al. describe that HM1.24 antigen is a target for antibody based immunotherapy of multiple myeloma. See Ohtomo at page 583, lines 4 to 7 of the summary. Treon and Ohtomo, however, do not describe or suggest whether HM1.24 is a promising target for immunotherapy using dendritic cells. According to the Treon reference and the Ohtomo reference, HM1.24 is used for immune therapy (ADCC or CDC), which is completely different from a cancer vaccine in mechanism of action. Thus, there is no reasonable expectation of success to use HM1.24 for a cancer vaccine.

More specifically, immune reactions in immunotherapy of cancers are classified in two groups, an antibody reaction and a T cell reaction. For example, Evans *et al.* at p. 299, left column, second paragraph describes that "[t]he immune response can be crudely divided into either antibody responses or T cell responses. Antibodies recognized and bound to conformational determinants on cell surface proteins can kill a cell by either antibody dependent cellular cytotoxicity or complement mediated cell lysis. Conversely, T cells recognize small proteins presented on the cell surface on MHC antigens, and T cell activation requires a co-stimulatory signal which is usually present on the cell surface of antigen presenting cells. Thus, the mechanism by which an immune reaction is caused is different depending on the type of immunotherapy.

The present application describes a cancer vaccine that causes an immune reaction through a T cell mechanism, and not ADCC or CDC, like Treon and Ohtomo. Thus, the combination of Treon and Ohtomo does not result in a cancer vaccine, *i.e.*, a composition that causes a T cell mediated immune reaction. Further, in view of the completely independent mechanisms of action, one of ordinary skill in the art would not have had any reasonable expectation of success that references could be combined across the distinct mechanisms.

Furthermore, while Porgador describes dendritic cells pulsed with a class I restricted peptide, one of skill in the art could not assume that a dendritic cell could be pulsed with HM1.24 antigen or that a dendritic cell pulsed with HM1.24 that operates through a T-cell mediated immune response would be suitable for treating a cancer based on prior art which indicates that antibody therapy could be used to treat multiple myeloma. The mechanism by

which an antibody and a dendritic cell cause an immune reaction are so different that success with one does not correlate with success with the other.

Indeed, when dendritic cells are pulsed with completely different peptides, success cannot be expected at all, whether or not CTL peptide specificity causes lysis of the target cells. Soluble peptides used to pulse dendritic cells in the Progador reference are ova peptides and mut-1 peptides (p. 256, left column, lines 21-28). On the other hand, as recognized by the examiner, the soluble peptide described in Ohtomo is HM1.24 soluble peptide. Although both sets of peptides are soluble, their sequences are completely different and therefore, the dendritic cells are pulsed with completely different peptides. Accordingly, it cannot be expected (whether or not a CTL peptide specifically causes lysis of the target cells) that the allegedly taught composition would cause lysis of the target cells by dendritic cells pulsed with HM1.24 peptide or protein.

Furthermore, Progador states that "[t]he concern was raised that certain methods of immunization will elicit only low affinity CTL that may be capable of recognizing targets presenting Ag in a physiological manner" (see Progador at page 257, left column, lines 39-46). This description teaches a person with ordinary skill in the art that there is no reasonable expectation of success to pulse the dendritic cells with the HM1.24 peptide.

In view of the foregoing, applicants respectfully request the rejections be withdrawn.

CONCLUSION

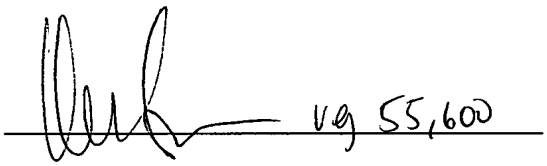
Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

Examiner Sang is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date November 29, 2007

By  Reg 55,600

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